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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/077,173	11/12/98	COMMUNI D	VANNA83.001A

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EXAMINER	
MURPHY, J	
ART UNIT	**PAPER NUMBER**
1644	10

DATE MAILED: 04/05/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/077,173	COMMUNI ET AL.	
	Examiner	Art Unit	
	Joseph F Murphy	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

1)☒ Responsive to communication(s) filed on *14 March 2000* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *70-90* is/are pending in the application.

4a) Of the above claim(s) *81-83,85-88 and 90* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *70-80,84 and 89* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a)☐ All b)☐ Some * c)☐ None of the CERTIFIED copies of the priority documents have been:

1.☐ received.

2.☐ received in Application No. (Series Code / Serial Number) _____ .

3.☒ received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

Attachment(s)

14) ☒ Notice of References Cited (PTO-892)
15) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
16) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 3 .
17) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
18) ☐ Notice of Informal Patent Application (PTO-152)
19) ☒ Other: *Sequence Comparison A* .

DETAILED ACTION

1. This application is a 371 of PCT/BE96/00123.

Election/Restrictions

2. Applicant's election with traverse of claims 70-80, 84 and 89 in Paper No. 9, 3/14/2000 is acknowledged. The traversal is on the ground(s) that a) although the Groups are patentably distinct, they contain overlapping subject matter; b) examination of all pending claims would not place a burden on the examiner. This is not found persuasive because a search of Group I which comprises the receptor, polynucleotide encoding the receptor, vector, host cell and method of compound screening would not reveal art on the inventions of the other Groups, i.e., an antibody ligand, a nucleotide analogue ligand, a method of hybridization or an anti-ligand. The separate field of search required for each Group would thus impose a burden on the examiner. The Restriction Requirement set forth in Paper No. 8, 2/9/2000, is still deemed proper and is therefore made FINAL.

3. Claims 81-83, 85-88 and 90 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

4. Claims 70-80, 84 and 89 are under consideration.

Specification

5. This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

6. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

The following title is suggested: Human pyrimidine receptor.

7. The first line of the specification must contain references to the priority documents.

Claim Rejections - 35 USC § 112 first paragraph

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8a. Claims 70-79, 84 and 89 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a substantially purified polypeptide comprising an amino acid sequence set forth in SEQ ID NO: 2, and encoded by a polynucleotide as set forth in SEQ ID NO: 1, does not reasonably provide enablement for an isolated receptor variant having at least 60% amino acid sequence homology with SEQ ID NO: 2, or encoded by a polynucleotide having more than 60% sequence homology to the polynucleotide as set forth in SEQ ID NO: 1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 70, 74, 84 and 89 are overly broad in the recitation of "having more than 60% sequence homology" since no guidance is provided as to which of the myriad of polypeptide species encompassed by the claim will retain the characteristics of a receptor having a preference for pyrimidine nucleotides over purine nucleotides. In the specification, no actual or prophetic examples on expected performance parameters of any of the possible muteins of the receptor are disclosed. It is known in the art that even single amino acid changes or differences in the amino acid sequence of a protein can have dramatic effects on the protein's function. For example, Mikayama et al. (1993) teaches that the human glycosylation-inhibiting factor (GIF) protein differs from human migration inhibitory factor (MIF) by a single amino acid residue (page 10056, Figure 1). Yet, despite the fact that these proteins are 90% identical at the amino acid level, GIF is unable to carry out the function of MIF, and MIF does not exhibit GIF bioactivity (page 10059, second column, third paragraph). It is also known in the art that a single amino

acid change in a protein's sequence can drastically affect the structure of the protein and the architecture of an entire cell. Voet et al. (1990) teaches that a single Glu to Val substitution in the beta subunit of hemoglobin causes the hemoglobin molecules to associate with one another in such a manner that, in homozygous individuals, erythrocytes are altered from their normal discoid shape and assume the sickle shape characteristic of sickle-cell anemia, causing hemolytic anemia and blood flow blockages (pages 126-128, section 6-3A and page 230, column 2, first paragraph).

There is no guidance provided in the specification as to how one of ordinary skill in the art would generate either a nucleic acid sequence encoding an a receptor having a preference for pyrimidine nucleotides over purine nucleotides, or a receptor polypeptide that has a preference for pyrimidine nucleotides over purine nucleotides, other than those exemplified in the specification. See In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404. The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. The factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: (1) the breadth of the claims; (2) the nature of the invention; (3) the state of the prior art; (4) the level of one of ordinary skill; (5) the level of predictability in the art; (6) the amount of direction provided by the inventor; (7) the existence of working examples; and (8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. Given the breadth of claims 70-79, 84 and 89 in light of the predictability of the art as determined by the number of working examples, the level of skill of the artisan, and the guidance provided in the instant specification and the prior art of record, it would require undue experimentation for one of ordinary skill in the art to make and use the claimed invention. Claims 71-73 and 75-79 are rejected insofar as they depend on the recitation of "having more than 60% sequence homology".

8b. Claim 75 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one

skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Due to the limitation of "genomic DNA" recited in the claim, a determination of what the claim as a whole covers indicates that elements which are not particularly described, e.g. promoters, enhancers, untranslated regions and introns, are encompassed by this claim. There is no actual reduction to practice of the claimed invention, or complete detailed description of the structure. A biomolecular sequence described only by a functional characteristic, in this case an isolated genomic nucleic acid encoding a receptor having a preference for pyrimidine nucleotides over purine nucleotides, without any known or disclosed correlation between that function and the structure of the sequence is not a sufficient identifying characteristic. See University of California v. Eli Lilly and Co. 43 USPQ2d at 1406. There is no known or disclosed correlation between this function and the structure of the non-described regulatory elements and untranslated regions of the genomic DNA. Weighing all factors in view of the level of knowledge and skill in the art, one skilled in the art would not recognize from the disclosure that the Applicant was in possession of the claimed invention.

8d. Claim 80 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 80 defines a nucleic acid probe by a function alone, i.e. it specifically hybridizes and prevents translation. However, in University of California v. Eli Lilly, 119 F.3 at 1568, 43 USPQ2d at 1406. the Court decided that a definition by function

alone "does not suffice" to sufficiently describe a nucleic acid sequence "because it is only an indication of what the gene does, rather than what it is." Further, "it is only a definition of a useful result rather that a definition of what achieves that result...The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention". Applicant has not set forth within the claim the detailed constitution of the nucleic acid probe, and thus does not satisfy the written description requirement.

Claim Rejections - 35 USC § 112 second paragraph

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9a. Claim 80 recites the term "specifically hybridize", which is a conditional term and renders the claim indefinite. Furthermore, some nucleic acids which might hybridize under conditions of moderate stringency, for example, would fail to hybridize under conditions of high stringency. The metes and bounds of the claim thus cannot be ascertained. This rejection could be obviated by supplying specific conditions, supported by the specification, which Applicant considers to be "specific".

9b. Claim 80 recites "the nucleic acid molecule of Claim 73". This is vague and indefinite in that claim 73 is drawn to a receptor, not a nucleic acid. For the sake of examination, the claim was read to refer to SEQ ID No: 1.

9c. The term "unique" in claim 80 is a relative term which renders the claim indefinite. The term "unique" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree of uniqueness, and one of skill in the art would not be reasonably apprised of the scope of the invention. Therefore the metes and bounds of this claim cannot be determined.

9d. The recitation of "included" in claim 80 renders the claim vague and indefinite, because it is unclear whether the term refers to an exogenous sequence that is cloned into the nucleic acid, or a particular sequence already present within the sequence.

9e. The term "preference" in claims 70, 80 and 84 is a relative term which renders the claim indefinite. The term "preference" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10a. Claim 80 is rejected under 35 U.S.C. 102(b) as being anticipated by Parr et al. (1994).

Parr et al. discloses a polynucleotide sequence that comprises more that 15 nucleotides that are identical to a region of SEQ ID NO:1 and are thus capable of hybridizing to SEQ ID NO: 1 (page 3276, Figure 1; see Sequence Comparison A, underlined region, attached) in the absence of a recitation of specific hybridization conditions in the claim.

Conclusion

11. No claim is allowed.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph F. Murphy whose telephone number is 703-305-7245. The examiner can normally be reached on M-F 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 703-308-3973. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-308-0294 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Joseph F. Murphy, Ph. D.
Patent Examiner
Art Unit 1644
April 3, 2000

Prema Mertz
PREMA MERTZ
PRIMARY EXAMINER